PTO/SB/17 (10-02)
Approved for use through 10/31/2002. OMB 0651-0032
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
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FEE TRANSMITTAL for FY 2003

Patent fees are subject to annual revision.

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($)375.00

Complete if Known	
Application Number	09/817,229
Filing Date	March 27, 2001
First Named Inventor	Ferguson *et al.*
Examiner Name	Chernyshev, O.
Group Art Unit	1646
Attorney Docket No.	1669.0040001/SRL/BLS

METHOD OF PAYMENT (check all that apply)

☐ Check ☒ Credit card ☐ Money Order ☒ Other** ☐ None

** Charge any deficiencies or credit any overpayments in the fees or fee calculations of Parts 1, 2 and 3 below to Deposit Account No. 19-0036.

☐ Deposit Account
Deposit Account Number 19-0036

Deposit Account Name: Sterne, Kessler, Goldstein & Fox P.L.L.C.

The Commissioner is authorized to: (*check all that apply*)

☐ Charge fee(s) indicated below ☐ Credit any over payments

☐ Charge any additional fee(s) during the pendency of this application

☐ Charge fee(s) indicated below, **except for the filing fee** to the above-identified deposit account.

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	750	2001	375	Utility filing fee	
1002	330	2002	165	Design filing fee	
1003	520	2003	260	Plant filing fee	
1004	750	2004	375	Reissue filing fee	
1105	160	2005	80	Provisional filing fee	

SUBTOTAL (1) ($) -0-

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

	Extra		Fee from below		Fee Paid
Total Claims ____ - 20** =	____	X	____	=	
Indep. Claims ____ - 3** =	____	X	____	=	
Multiple Dependent	____			=	

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	18	2202	9	Claims in excess of 20
1201	84	2201	42	Independent claims in excess of 3
1203	280	2203	140	Multiple dependent claim, if not paid
1204	84	2204	42	**Reissue independent claims over original patent
1205	18	2205	9	**Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($) -0-

***or number previously paid, if greater; For Reissue, see above*

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1502	50	2052	25	Surcharge-late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	110	2251	55	Extension for reply within first month	
1252	410	2252	205	Extension for reply within second month	
1253	930	2253	465	Extension for reply within third month	
1254	1,450	2254	725	Extension for reply within fourth month	
1255	1,970	2255	985	Extension for reply within fifth month	
1401	320	2401	160	Notice of Appeal	
1402	320	2402	160	Filing a brief in support of an appeal	
1403	280	2403	140	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	110	2452	55	Petition to revive - unavoidable	
1453	1,300	2453	650	Petition to revive - unintentional	
1501	1,300	2501	650	Utility issue fee (or reissue)	
1502	470	2502	235	Design issue fee	
1503	630	2503	315	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	750	2809	375	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	750	2810	375	For each additional invention to be examined (37 CFR 1.129(b))	
1801	750	2801	375	Request for Continued Examination (RCE)	375
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) ____

* Reduced by Basic Filing Fee Paid

SUBTOTAL (3) ($)375.00

SUBMITTED BY

Complete *(if applicable)*

Name (Print/Type)	Bryan L. Skelton	*Registration No. (Attorney/Agent)*	50,893	*Telephone*	202-371-2600
Signature				*Date*	April 21, 2003

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

Sterne Kessler Goldstein Fox
ATTORNEYS AT LAW

April 21, 2003

WRITER'S DIRECT NUMBER:
(202) 772-8769
INTERNET ADDRESS:
bskelton@skgf.com

Commissioner for Patents
Washington, D.C. 20231

Art Unit 1646
Box RCE

Re: U.S. Utility Patent Application
Appl. No. 09/817,229; filed March 27, 2001
For: **Method for Effecting Neuroprotection**
Inventors: Ferguson *et al.*
Our Ref: 1669.0040001/SRL/BLS

Sir:

Transmitted herewith for appropriate action are the following documents:

1. Fee Transmittal (Form PTO/SB/17);

2. Request for Continued Examination (RCE) Transmittal (Form PTO/SB/30);

3. Supplemental Reply;

   a. Goldberg, M.R., *et al.*, "Biochemical Effects of Losartan, a Nonpeptide Angiotensin II Receptor Antagonist, on the Renin-Angiotensin-Aldosterone System in Hypertensive Patients," *Hypertension 25*:37-46, American Heart Association, Inc. (1995); and

   b. Gradman, A.H., *et al.*, "A Randomized, Placebo-Controlled, Double-Blind, Parallel Study of Various Doses of Losartan Potassium Compared With Enalapril Maleate in Patients With Essential Hypertension," *Hypertension 25*:1345-1350, American Heart Association, Inc. (1995);

4. Return postcard; and

5. Credit Card Payment Form PTO-2038 for $375.00 to cover the fee for filing a request for continued examination (37 C.F.R. § 1.17(e)).

It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Bryan L. Skelton
Agent for Applicants
Registration No. 50,893

BLS/dab
::ODMA\MHODMA\SKGF_DC1;125097;1
Enclosures

PTO/SB/30 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

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REQUEST FOR CONTINUED EXAMINATION (RCE) TRANSMITTAL

Subsection (b) of 35 U.S.C. § 132, effective on May 29, 2000, provides for continued examination of an utility or plant application filed on or after June 8, 1995. See The American Inventors Protection Act of 1999 (AIPA).

Application Number	09/817,229
Filing Date	March 27, 2001
First Named Inventor	Ferguson *et al.*
Group Art Unit	1646
Examiner Name	Chernyshev, O.
Attorney Docket Number	1669.0040001/SRL/BLS

This is a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114 of the above-identified application.

NOTE: *37 C.F.R. § 1.114 is effective on May 29, 2000. If the above-identified application was filed prior to May 29, 2000, applicant may wish to consider filing a continued prosecution application (CPA) under 37 C.F.R. § 1.53 (d) (PTO/SB/29) instead of a RCE to be eligible for the patent term adjustment provisions of the AIPA.* See *Changes to Application Examination and Provisional Application Practice*, Interim Rule, 65 *Fed. Reg.* 14865 (Mar. 20, 2000), 1233 *Off. Gaz. Pat. Office* 47 (Apr. 11, 2000), which established RCE practice.

1. Submission required under 37 C.F.R. § 1.114
   - a. ☒ Previously submitted
     - i. ☒ Consider the amendment(s)/reply under 37 C.F.R. § 1.116 previously filed on February 20, 2003. (Any unentered amendment(s) referred to above will be entered).
     - ii. ☐ Consider the arguments in the Appeal Brief or Reply Brief previously filed on _____
     - iii. ☐ Other _____
   - b. ☒ Enclosed
     - i. ☒ Supplemental Amendment/Reply
     - ii. ☐ Affidavit(s)/Declaration(s)
     - iii. ☐ Information Disclosure Statement (IDS)
     - iv. ☐ Other _____
2. Miscellaneous
   - a. ☐ Suspension of action on the above-identified application is requested under 37 C.F.R. § 1.103(c) for a period of _____ months. (Period of suspension shall not exceed 3 months; Fee under 37 C.F.R. § 1.17(i) **required**)
   - b. ☐ Other _____
3. Fees The RCE fee under 37 C.F.R. § 1.17(e) is required by 37 C.F.R. § 1.114 when the RCE is filed.
   - a. ☒ The Director is hereby authorized to charge the following fees, or credit any overpayments, to Deposit Account No. 19-0036
     - i. ☒ RCE fee required under 37 C.F.R. § 1.17(e)
     - ii. ☐ Extension of time fee (37 C.F.R. §§ 1.136 and 1.17)
     - iii. ☐ Other _____
   - b. ☐ Check in the amount of $_____ enclosed
   - c. ☒ Payment by credit card (Form PTO-2038 enclosed)

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT REQUIRED

Name (Print /Type)	Bryan L. Skelton STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.	*Registration No. (Attorney/Agent)*	50,893
Signature		*Date*	April 21, 2003

CERTIFICATE OF MAILING OR TRANSMISSION

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner For Patents, Box RCE, Washington, DC 20231, or facsimile transmitted to the U.S. Patent and Trademark Office on:

Name(Print/Type)			
Signature		*Date*	

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND Fees and Completed Forms to the following address: Commissioner for Patents, Box RCE, Washington, DC 20231.

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SKGF Rev. 10/20/00 mac

#18/Ryu

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: 8063
Ferguson *et al.*	Art Unit: 1646
Appl. No. 09/817,229	Examiner: Chernyshev, O.
Filed: March 27, 2001	Atty. Docket: 1669.0040001/SRL/BLS
For: **Method for Effecting Neuroprotection**	

Supplemental Reply

Commissioner for Patents
Washington, D.C. 20231

Sir:

In the previous Amendment and Reply filed on February 20, 2003, Applicants provided excerpts from several cited U.S. patents as well as from the Physician's Desk Reference (PDR). The references teach effective dose ranges of angiotensin II receptor antagonists for the control of blood pressure in hypertensive patients. None of the references suggests the present method's use of angiotensin II receptor antagonists for preventing damage to the excitable cells of a patient who is undergoing or has undergone an ischemic event.

The above references support the enablement of one of ordinary skill in the art to practice the claimed method. The Examiner correctly points to the fact that the reported dosing regimens in the above references in their original context do not purport to validate a method of preventing damage caused by an ischemic event. However, taken together with Applicants' *in vivo* experiments showing veracity of the claimed method, a skilled artisan, without undue experimentation, will be able to routinely interpret dose ranges to develop a therapeutic index for the practice of the claimed valid method. Further, the data published in the PDR show therapeutic ranges and overdosages. Thus, the references

support enablement because the reported data demonstrate the predictability of the range of efficacious doses of angiotensin II receptor antagonists.

Because the references do not suggest the use of angiotensin II receptor antagonists for the claimed method, the Examiner erred in her interpretation of the relevance of the PDR reference (Exhibit B). The claimed method is for preventing damage to the excitable cells of a patient who is undergoing or has undergone an ischemic event. Such an event is not hypertensia, although hypertensia may lead to an ischemic event. An ischemic event is an event in which the blood supply to a tissue is obstructed, such as during stroke or myocardial infarction. In addition to hypertensia, an ischemic event may result from other pathologies such as hemorrhage, thrombosis or embolism. The reference does not teach or fairly suggest administration of the angiotensin II receptor antagonist, losartan, during or following an ischemic event. Rather, losartan is indicated for use in hypertensia. Thus, the present method is in no way prejudiced by the teachings of the reference.

Applicants submit herewith two peer-reviewed journal articles, (1) Goldberg, M.R., *et al.*, "Biochemical Effects of Losartan, a Nonpeptide Angiotensin II Receptor Antagonist, on the Renin-Angiotensin-Aldosterone System in Hypertensive Patients, *Hypertension 25*:37-46, American Heart Association, Inc. (1995); and (2) Gradman, A.H., *et al.*, "A Randomized, Placebo-Controlled, Double-Blind, Parallel Study of Various Doses of Losartan Potassium Compared with Enalapril Maleate in Patients With Essential Hypertension," *Hypertension 25*:1345-1350, American Heart Association, Inc. (1995). These references are directed to the routine practice and predictability of clinical administration of angiotensin II receptor antagonists. Neither of these references teaches

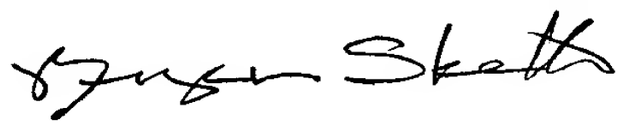
or even suggests administering angiotensin II receptor antagonists to a patient during or after an ischemic event. Applicants respectfully request that the Examiner consider these references.

Based on the above remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Prompt and favorable consideration of this Supplemental Reply is respectfully requested. Applicants believe the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Bryan L. Skelton
Agent for Applicants
Registration No. 50,893

Date: April 21, 2003

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